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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/895,381	07/02/2001	Douglas C. Stahl	2703.2	1421

5514 7590 01/12/2004

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EXAMINER	
CLOW, LORI A	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 01/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M. S.M.

Office Action Summary	Application No.	Applicant(s)	
	09/895,381	STAHL, DOUGLAS C.	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' arguments, filed 02 October 2003, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-48 are currently pending.

Claim Objections

In the Office Action dated 03 June 2003, claims 25-36 were objected to for being substantial duplicates of claims 1-12. Applicant's arguments with respect to this objection are persuasive and the objection is hereby withdrawn.

Petition to Accept Color Photographs

The petition to request acceptance of color drawings has not yet been decided. A decision will be forthcoming.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Utility

Claims 1-48 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The claims recite a method for interpreting data comprising transforming data

and obtaining sequence information. The specification teaches that transformation of data can be used for identification of patterns for the establishment of a particular genotype (page 4, lines 22-25). However, the claimed method is not directed to the steps of pattern identification for the purpose of genotyping. It is merely directed to transforming data that represent nucleic acid data. The specification does not teach any specific, substantial, or well-established utility for a method that simply transforms nucleic acid data. Use of the claimed method to analyze the data such that patterns are identified is certainly of scientific interest; however, no specific, substantial, and credible utility is set forth for the mere transformation of data as the "use" gained from this transformation is not disclosed or claimed. Utilities that require further research to identify or reasonably confirm a real-world context of use are not substantial utilities (See MPEP 2107.01). Therefore the claimed method does not have utility.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a

determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims

In considering the factors for the instant claims:

a) and e) In order to practice the claimed invention one of skill in the art must be able to interpret nucleic acid data by obtaining the data, transforming the data, and obtaining sequence information from the transformed data. However, the methods of claims 1-48 are not enabled as the claims and the specification are lacking critical steps and information required for the performance of said methods. One of skill in the art would not be able to perform the invention as claimed and the steps as presently recited would not result in obtaining the desired information from the methods.

For example, in claim 1 how is the data transformed from a spatial domain to a frequency domain? Does any transformation method suffice? Furthermore, what is being transformed? The individuals of the base sequence? The specification, at page 9, indicates that Hadamard, Fourier, and Wavelet transformation is used, but is silent as to other methods amenable to the method. However, claim 1 reads on ANY transformation to the data.

Once the data are transformed, it is unclear how sequence information is gained through data mining. There is no comparison step such that sequence information would be generated. For instance, in BLAST sequence alignment data mining tools, sequences are compared to known sequences in order to formulate similarities between sequences. Would any known data mining technique work such that significant sequence information is obtained? The specification only

indicates the use of a CART algorithm. Furthermore, what type of sequence information is obtained? Similarity, identity, or some other characteristic? Or is the sequence data obtained the actual base sequence data? An obtained value on its own, with no reference or baseline value tells one nothing of its significance. The claims do not have any such steps wherein values are compared and significance concretely defined and gained.

Claim 1 requires "interpreting data", however, there is no step of interpreting data and the parameters such that one would do so are not outlined. It is unclear if only sequence data is needed or required or some other types of data are utilized. The specification does not clearly address this issue.

One would look to the art to practice the invention. However, the art describes detailed steps to perform sequence data analysis. However, the claimed methods do not provide such detailed steps and it is therefore not possible to practice said invention without undue experimentation.

b) and c) The specification provides no working examples of using the particular method.

d) The invention is drawn to interpreting data from nucleic acids by data transformation and data mining.

f) The skill of those in the art of bioinformatics is high.

g) The art is unpredictable.

h) The claims are broad because they are drawn to methods with all nucleic acids, all transformation techniques and all data mining techniques.

The skilled practitioner would first turn to the instant specification for guidance to practice the claimed methods. However, the instant specification does not provide specific

guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art does not teach these methods for use with all possible transformation techniques and all data mining techniques. Finally, said practitioner would turn to trial and error experimentation to determine the limits and steps required. Such represents undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 13, 25, and 37 recite a "method of interpreting data" in the preamble, however there is no interpretation step in the remaining portion of the claim.

Claims 1, 13, 25, and 27 recite "transformation" of data. However, it is unclear what type of transformation is being performed. Is it transformation into signals, amps, or light wavelengths, for example?

Claim 1 recites "executing a data mining process on the transformed data". It is unclear what data mining process is intended. Is the data mining process a pattern finding process or some other process?

Claim 2 recites "performing a process". However, it is unclear what process is being performed on the image. Is it an image enhancement process or a process by which the image is transformed into digital or analog data?

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 5-9, 13-15, 17-21, 25-27, 29-33, 37-39 and 41-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ewing et al. (Genome Research (1998) Vol. 8, pages 175-185) in view of Youssef (A Lecture Series on Data Compression (translation 1996 by Speilman@NIST.GOV) pages 1-9).

As stated in the previous Office Action, Ewing et al. present an automated process for sequence data processing called *Phred.* In the analysis a gel image containing nucleic acid data is converted to an inferred base sequence (or read) for each template. The analysis consists of four distinct steps: lane tracking, in which lane boundaries are identified; lane profiling, in which each of the four signals is summed across the lane width to create a profile, or trace, consisting of a set of four arrays indicating signal intensities at several thousand uniformly

spaced time points during the gel run; trace processing, in which signal processing methods are used to deconvolve and smooth signal estimates, reduce noise, and correct for dye effects on fragment mobility and for long-range electrophorectic trends; and base-calling, in which the processed trace is translated into a sequence of bases (page 175, column 2). As required by claim 1, Ewing et al. describe a system in which nucleic acid data is in the form of a spatial domain (gel), data is transformed (mined), and sequence data is obtained. Furthermore, the spatial domain data is gained from gel electrophoresis and a machine-readable format is gathered from the image in the form of a chromatogram (page 176, column 1), as required by claim 2. The goal of the software is to actually produce a sequence as accurate as possible despite data problems, such as compressions, weak or variable signals, and trace spacing. This involves data normalization, as described in detail on pages 176, column 2 and 177, column 1 and required by claim 3. The transformation performed involves the use of the Fourier transformation, as required by claim 6, 18, 30, and 42 (see page 177, column 2).

Ewing et al. do not teach the use of specific data transformation algorithms as in claims 5-9, 17-21, 29-33, and 41-45, however Youssef does speak on data transformation techniques. The lecture includes an overview of various methods of data compression that are utilized in a variety of areas such that data is decorrelated so that fast scalar quantization can be used (page 1). The methods that are typically used include Fourier transformation, wavelet transformation and Hadamard transformation (page 1). It would have been prima facie obvious to one of skill in the art to use the various data transformation techniques in the data transformation process of Ewing et al., as motivated by the fact that these manipulations improve accuracy. Ewing, at page 184, speaks of this improvement in accuracy as needed in the future for high-quality traces.

Claims 1-3, 10-15, 22-27, 34-39 and 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ewing et al. (Genome Research (1998) Vol. 8, pages 175-185) in view of Curram et al. (Journal Opl Res. Soc. (1994) Vol.45, pages 440-450), as supported by Ma et al. (International Journal on Artificial Intelligence Tools (1993) pages 1-19).

Ewing et al. also do not teach the use of neural networks and classification trees to data mine the transformed data. However, Curram et al. describe a comparison of classification methods which are applicable for classification tasks, such as required by the instant claims 10-12, 22-24, 34-36, and 46-48. Curram describes that neural networks were used to establish relationships between sets of variables. Not only have neural networks been instrumental in investigating how the brain operates, but they have been exploited for their mathematical properties as signal processors (which applies to the instant use) and non-linear statistical models (page 440, 4th paragraph). The most common network is known as a back propagation network, as in claim 11, which is a layered network with an input layer, hidden layers, and an output layer. This system uses supervised learning in which examples are presented to the network along with their target outputs.

Curram et al. also describe induced rule trees for data mining which include CART. These techniques are useful when data are not deterministic but uncertain (page 443, 3rd paragraph), as could easily be applied to biological sequence data. The uncertainty may be due to noise in the measurements or to the presence of factors which cannot be measured, which could also be applied to sequence data. It would have been prima facie obvious to one of skill in the art to utilize known data mining techniques such as those of Curram, in the methods of Ewing where the motivation is to further assess the data transformed by the method of Ewing et

that biological data mining was growing and that extraction of significant data was important to understand relationships among sequences, genes, proteins etc. (see as a review Ma et al. International Journal on Artificial Intelligence Tools (1993) pages 1-19).

Claims 1-4, 13-16, 25-28, and 37-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ewing et al. (Genome Research (1998) Vol. 8, pages 175-185), in further view of Allex et al. (Bioinformatics (1999) Vol. 15, pages 723-728).

Ewing et al. do not teach the spatial domain comprising size versus intensity. However, Allex et al. do teach a neural network for sequence analysis which analyzes input features containing information of size versus intensity, as in claims 4, 16, 28, and 40 (page 724, column 2-page 725, column 1). It would have been prima facie obvious to one of ordinary skill in the art to utilize Allex's features in sequence analysis in the method of Ewing. The motivation to do so comes from Allex et al. on page 728, who state that neural networks can be an effective tool for determining the consensus of aligned DNA sequences for better accuracy.

Applicants Arguments

Applicant argues that "as described in the specification the transformation of the nucleic acid data from the spatial domain to the frequency domain minimizes "within-class" variability and maximizes "between-class" variability of features of interest, such as allele patterns". Furthermore, "the transformation to the frequency domain removes or reduces redundancies in the pattern recognition process, and, additionally, the amount of data subjected to the data mining process is reduced so as to increase the efficiency of the pattern recognition process."

While this may be present in the specification, the claims are not directed to such limitations and the above art still reads on the claimed subject matter.

Applicant further argues that the nucleic acid data of Ewing et al. is not transformed. However, this is not persuasive. Ewing et al. clearly transform data by using Fourier methods, as stated above. These methods are known in the art to transform spatial data to frequency data, as evidenced above by Youssef.

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

Lori A. Clow
AU 1631
January 5, 2004

MARJORIE MORAN
PATENT EXAMINER